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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/685,432	10/10/2000	Jay M. Short	DIVER1280-3	4977

7590 08/22/2003

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EXAMINER
EPPERSON, JON D

ART UNIT	PAPER NUMBER
1639	21

DATE MAILED: 08/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
File Copy	09/685,432	SHORT ET AL.	
	Examiner	Art Unit	
	Jon D Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-61* is/are pending in the application.

4a) Of the above claim(s) *21 and 27-61* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20 and 22-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5,7,10,1* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

1. Receipt is acknowledged of a Response to a Restriction Requirement, which was dated on May 20, 2003 (Paper No. 19).

Status of the Claims

2. Claims 1-61 are pending in the present application.

3. Applicants' response to the Restriction and/or Election of Species requirements in Paper No. 7 is acknowledged (Applicants elected Group I, claims 1-26) and claims 27-61 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim (see below i.e., ***Response to Restriction and/or Election of Species***).

4. Please note: Applicant's elected species (thermophile, erythromycin, expression library, fluorescein, FACS, C12FDG, metabolic pathway) were found in the art, see rejections below. Applicant is reminded of MPEP § 803.02 with respect to species elections:

> On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a nonelected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. ***The prior art search, however, will not be extended unnecessarily to cover all nonelected species.*** Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended Markush-type claim will be reexamined. The prior art search will be extended to the extent necessary to determine

patentability of the Markush-type claim. In the event prior art is found during the reexamination that anticipates or renders obvious the amended Markush-type claim, the claim will be rejected and the action made final. Amendments submitted after the final rejection further restricting the scope of the claim may be denied entry.

5. Claim 21 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected species, the requirement having been traversed in Paper No. 6 (see below i.e., ***Response to Restriction and/or Election of Species***).

6. Therefore, claims 1-20 and 22-26 are examined on the merits in this action.

Response to Restriction and/or Election of Species

7. Applicant's election of Group I (claims 1-26) in Paper No. 13 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)) (see Paper No. 15, paragraph 1).

8. Applicant's election of species with traverse in Paper Nos. 16 and 19 is also acknowledged.

9. The election of species traversal is on the ground(s) that **[1]** the claimed subject matter in each group is related by a "commonality of operation, function and effect" according to MPEP § 806.04(e), such that an election of a single species is improper (see Paper No. 16, page 2, paragraph 1), **[2]** if the search can be made without serious burden the examiner must examine it

on its merits according to MPEP § 803 (see Paper No. 16, page 2, paragraph 1), **[3]** all "extremophiles" share a commonality because the survive under extreme conditions and, as a result, there is no undue burden on the examiner (see Paper No. 16, page 2, paragraph 2), **[4]** search of different microenvironments is not burdensome on the examiner because all share the common characteristic of allowing encapsulation and thus the species election should be withdrawn pursuant to MPEP § 806.04(e) (see Paper No. 16, page 3, paragraph 1), **[5]** search of different polynucleoitdes of interest would not be burdensome because they also are related i.e., they all encode for a protein (see Paper No. 16, page 3, paragraph 2), **[6]** "all of the methods for high throughput screening of a library of polynucleotides will have to be searched multiple times. Thus, the Examiner will be required to search the same group of references over and over again, causing much waste of time and energy" (see Paper No 19, page 2, paragraph 1), **[7]** "Applicants will be required to file and prosecute multiple applications, entailing much delay and cost that could be avoided by rejoining the species in the claims" (see Paper No 19, page 2, paragraph 1) and **[8]** "Applicant's invention is based on screening a library of clones that encode an activity of interest, rather than the device that is utilized for the screening or the fluorescent molecule or reporter system that is used. Any type of flow cytometry device or fluorescent molecule would be useful in the claimed invention and would not require a separate search" (see Paper No. 19, page 3).

10. These arguments were fully considered but were not found persuasive. The Examiner's position is that **[1-5]** that the "commonality of operation, function and effect" that Applicants refer to for the elected species represent only the most tenuous of relationships and do not merit

consideration under MPEP § 806.04(e). Furthermore, the Examiner asserts assuming arguendo that even if there was legitimate overlapping subject matter the searches would not be coextensive because there is also non-overlapping subject material and, as a result, the searches would not be coextensive and, as a result, would be burdensome as outlined in Paper No. 15). **[6]** there is no basis for the assertion that all of the methods would have to be searched "multiple times" and even if *assuming arguendo* that the methods did have to be searched "multiple times" this assertion is not relevant to the requirements of a species election (i.e., the Examiner only needs to show that the species are distinct and burdensome to search, see MPEP § 802-803). Furthermore, **[7]** there is also no basis for the assertion that Applicants would have to "file and prosecute multiple application, entailing much delay and cost" because it was already stated in Paper No. 4 that "Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141" (see Restriction Requirement, page 9, paragraph 14). Finally, **[8]** the Examiner has already stated that "[s]hould applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case" (see Restriction Requirement, page 8, paragraph 12). This has not been done.

11. As a result, the restriction requirement and/or election of species is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

12. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98 (b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on the form PTO-892, they have not been considered.

Specification

13. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 1-20 and 22-26 are rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed,

had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 USC 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4 pages 1099-1111, Friday January 5, 2001. This is a written description rejection.

These claims encompass a broad genus. For example, claims 1-20 and 22-26 outline steps for identifying a bioactivity or a biomolecule of interest wherein no distinguishing features are provided for microenvironment (see claim 15), library containing a plurality of clones (see claim 1), mixed population of organisms (see claim 1), oligonucleotide probes (see claim 1), detectable molecule and bioactvity. The specification and claims do not place any limit on the number of atoms, the types of atoms, or the manner in which said atoms might be connected to form the microenvironment, clones, probes, and detectable molecules. This reads on an infinite number of possibilities and thus represents enormous scope. Consequently, there is simply no common attributes that can link together ***all*** of the microenvironments, clones, probes and markers i.e., there is no teaching that would allow a person of skill in the art to determine *a priori* ***all*** the different types of microenvironments, clones, probes and markers that should be screened and thus included in this enormous genus from the few examples provide by applicants.

The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify ***all*** of the members of the genus or even a substantial portion thereof, and because the genus is enormous and highly variant, listing one example of a library (e.g., see specification, Examples) is insufficient to teach the entire genus. Consequently, one of skill in the art would reasonably conclude that the disclosure

fails to provide a representative number of species to describe this enormous genus. Thus, applicant was not in possession of the claimed genus.

With respect to adequate disclosure Applicant is referred to the discussion in *University of California v. Eli Lilly and Co.* (U.S. Court of Appeals Federal Circuit (CAFC) 43 USPQ2d 1398 7/22/1997 Decided July 22, 1997; No. 96-1175) regarding disclosure. For adequate disclosure, like enablement, requires *representative examples*, which provide reasonable assurance to one skilled in the art that the compounds falling within the scope both possess the alleged utility and additionally demonstrate that *applicant had possession of the full scope of the claimed invention.* See *In re Riat*_(CCPA 1964) 327 F2d 685, 140 USPQ 471; *In re Barr* (CCPA 1971) 444 F 2d 349, 151 USPQ 724 (for enablement) and University *of California v. Eli Lilly and Co* cited above (for disclosure). The more unpredictable the art the greater the showing required (e.g. by "representative examples") for both enablement and adequate disclosure. Here, Applicants have not provided enough examples to show that they were in possession of the broad claims.

Furthermore, with regard to the description requirement, Applicants' attention is directed to The Court of Appeals for the Federal Circuit which held that a "written description on an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original)[The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)]. Here, the

"microenvironment" (see claim 15) is only described by its function i.e., its ability to encapsulate the clones. The Examiner contends that this functional language does not provide the requisite definition "such as by structure, formula [or] chemical name" that is required.

Claims Rejections - 35 U.S.C. 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

15. Claims 7, 8, 19 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. ***Claim 22*** recites "the polynucleotide of interest encodes a small molecule" in lines 1-2. The term "small" is a relative term, which renders the claim indefinite and/or unclear. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. See also MPEP § 2173.05(b).

Claims Rejections - 35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(e) the invention was described in-
(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

16. Claims 1-10, 12-20 and 22-26 are rejected under 35 U.S.C. 102(e) as being anticipated by Thompson et al (US Patent No. 5,824,485) (Filed **April 24, 1996**).

For ***claim 1***, Thompson et al (see entire document) discloses a method for screening molecular diversity, which anticipates claims 1. For example, Thompson et al discloses [a] contacting a library containing a plurality of clones comprising polynucleotides derived from a mixed population of organisms or more than one organism, with at least one oligonucleotide probe labeled with a detectable molecule (e.g., see Thompson et al, column 34, lines 62-65, "The present invention also provides encapsulation as an efficient high-throughput method for growing cells in a confined space"; see also column 35, paragraph 1; see also column 37, line 55; see also column 48, section 5.4.10; see also column 5, lines 38-41, "libraries can be used, the libraries can be further modified to incorporate a reporter regimen tailored to identify clones"; see also column 12, paragraph 3; see also column 27, paragraph 2; see also column 29, paragraph 1; see also column 32, paragraph 1; see also column 33, paragraph 1; see also column 12, paragraph 2; see especially column 25, paragraph 2, "Either DNA or RNA may be used as starting genetic material for preparing such libraries which may include cDNA libraries, genomic DNA libraries, as well as mixed cDNA/genomic DNA libraries, DNA

fragments derived from a plurality of donor organisms, e.g., organisms described in Section 5.1.1, are introduced into a pool of host organisms, such that each host organism in the pool contains a DNA fragment derived from one of the donor organisms"; see also Thompson et al, see section 5.2.3, especially column 37, lines 30-36, "The combinatorial gene expression libraries of the invention may be pre-screened or screened by a variety of methods, including but not limited to, visual inspection, automated image analysis, hybridization to molecular beacon DNA probes (Tyagi et al.1996, *Nature Biotechnol*, 14:303-308) fluorescence activated cell sorting (FACS) and magnetic cell sorting (MACS)"; section also section 5.2; see especially column 32, paragraph 1, "The preselected fragments of DNA contain genes encoding partial or complete biosynthetic pathways, and may be preselected by hybridizing to an initial DNA library a plurality of probes prepared from known genes that may be related to or are involved in producing compounds of interest"; see also column 32, lines 29-56; see also column 34, paragraphs 2-4; see especially column 34, lines 44-47; see also section 5.2.2. disclosing the use of fluorescent probes; see also column 33, line 38; see also column 37, line 35).

Furthermore, Thompson et al discloses [b] separating clones with an analyzer that detects the detectable molecule (see Thompson et al, column 33, line 39 e.g., disclosing the use of "FACS" analysis; see also column 37, line 35; see also column 35, paragraph 2, column 36, paragraph 2; see more generally section 5.2.2.; see also column 47, paragraph 1-7).

For ***claim 2***, Thompson et al discloses [a] contacting the separated clones with a reporter system that identifies a polynucleotide encoding the activity of interest (see

Thompson et al, column 5, paragraph 3, "While standard methods of screening gene expression libraries can be used, the libraries can be further modified to incorporate a reporter regimen tailored to identify clones that are expressing the desirable pathways and metabolic products [i.e., polynucleotides encoding the activity of interest]"; see also column 5, lines 55-65; see also abstract; see also figures 7-8, see also column 11, line 33-40).

Furthermore, Thompson et al discloses [b] identifying clones capable of modulating expression or activity of the reporter system thereby identifying a polynucleotide of interest (see Thompson et al, section 5.2.1.; especially column 35, lines 38-67 disclosing reporter constructs with inducible promoters; see also claims 17, 33; see also column 34, line 35; see also column 35, line 66).

For ***claim 3***, Thompson et al discloses an expression library (e.g., see Thompson et al, column 6, paragraph 4; see also column 5, paragraph 4, "standard methods of screening gene expression libraries can be used"; see also figures 1-2; see also column 9, paragraph 4).

For ***claim 4***, Thompson et al discloses a fluorescent molecule (see Thompson et al, column 35, paragraph 2; see also column 36, paragraph 2; see section 5.2.2., especially column 36, last two paragraphs, "A physiological probe as used herein is a fluorescent or colorigenic agent"; see also column 37, paragraphs 1-2).

For ***claim 5***, Thompson et al discloses FACS (see Thompson et al, column 7, line 2; see also figure 9; see also column 33, line 39; see also column 35, line 10).

For ***claim 6***, Thompson et al discloses a mixed population of organisms from an environmental sample (see Thompson et al, column 12, section 5.1.1. Donor Organisms, especially line 43, "Any organism can be a donor organism ... obtained from ... environmental samples").

For ***claim 7***, Thompson et al discloses microorganisms (e.g., see Thompson et al, see column 12, line 59, "the invention is not limited to microorganism donors).

For ***claims 8-9***, Thompson et al discloses extremophiles including thermophiles, acidophiles and halophiles (e.g., see Thompson et al, column 13, last paragraph; see especially column 14, line 2, "The donor organisms may be thermophilic, halophilic, acidophilic, barophilic, methanogenic").

For ***claim 10***, Thompson et al teaches reporter systems that are bioactive substrates (see Thompson et al, column 34, paragraphs 3-4, especially line 45; see especially column 36, last paragraph, "The probe can be an enzyme substrate"; see also column 47, line 28).

For ***claims 13-14***, Thompson et al discloses (a) obtaining polynucleotides from an population of organisms (see Thompson et al, column 12, lines 38-44, "Any organism can be a donor organism for the purpose of preparing a combinatorial gene expression library of the invention ... from environmental samples [i.e., a mixed population] either cultivable or uncultivable"; see also column 12, line 18). Thompson et al also discloses (b) normalizing the polynucleotides obtained from the sample and (c) generating a library from the normalized polynucleotides (see Thompson et al, column 32, lines 14-16, "all the positive clones can be pooled and used for making the biased [i.e., normalized]

combinatorial gene expression library. The initial library may be amplified so that DNA donor organisms can be pre-screened, and DNA from all of the positive clones can be pooled and used for making the biased combinatorial gene expression library"; see also column 32, line 54; see also more generally section 5.1.6; see also column 17, lines 48-62; see especially claims 3, 21).

For ***claims 15-17***, Thompson et al discloses encapsulation via a gel microdrop (e.g., see Thompson et al, column 38, line 15; see also column 38, line 38; see also column 37, line 57).

For ***claims 18-19***, Thompson et al discloses any enzyme and provides several examples including esterase (e.g., see Thompson et al, column 9, line 14; see also column 33, line 35; see also column 34, line 45; see also column 4, paragraph 2).

For ***claim 20***, Thompson et al discloses a detectable label (see Thompson et al, column 34, paragraphs 1-3; see also column 33, line 43).

For ***claim 22***, Thompson et al discloses "small" molecules (see Thompson et al, column 30, paragraphs 6-8; see also column 4, paragraph 2).

For ***claim 23-25***, Thompson et al discloses polynucleotides of interest comprise one or more operons (see Thompson et al, column 25, line 59; see especially column 26, last paragraph; see also column 36, paragraph 1; see most especially claim 9, "The gene expression library of claim 7 in which the cDNA or genomic DNA fragments comprise one or more operons, or portions thereof"). Thompson et al also discloses operons for the polketide syntheses (see Thompson et al, column 4, paragraph 2; see also column 13, paragraph 4, see also column 32, paragraph 3; see also column 60, paragraph 2; see also

column 60, second to lat paragraph). Thompson et al also discloses complete or incomplete metabolic pathways (see Thompson et al, column 32, paragraph 1, "The preselected fragments of DNA contain genes encoding partial or complete biosynthetic pathways, and may be preselected by hybridizing to an initial DNA library a plurality of probes prepared from known genes that may be related to or are involved in producing compounds of interest"; see also column 6, line 47 providing definition of metabolic pathway; see also figure 1).

For ***claim 26***, Thompson et al discloses FACS (see Thompson et al, column 7, line 2; see also figure 9; see also column 33, line 39; see also column 35, line 10).

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

19. Claims 1-20 and 22-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thompson et al (US Patent No. 5,824,485) (Filed **April 24, 1996**) and Miao et al (Miao, F.; Todd, P.; Kompala, D. S. "A single-cell assay of β-galactosidase in recombinant *E. coli* using flow cytometry" Biotechnology and Bioengineering (**1993**), 42, 708-715).

For ***claims 1-10, 12-20 and 22-26***, Thompson et al teaches all the limitations stated in the 35 U.S.C. 102(e) rejection above (incorporated in its entirety herein by reference), which anticipates claims 1-10, 12-20, 22-26 and, consequently, also renders obvious claims 1-10, 12-20 and 22-26.

The prior art teaching of Thompson et al differs from the claimed invention as follows:

For ***claims 11-12***, the prior art teachings of Thompson et al differs from the claimed invention by not specifically reciting the use of "C12FDG". Thompson et al implies that C12FDG may be used by reciting the use of β-galactosidase in the reporter system that uses C12FDG i.e., C12FDG is commonly hydrolyzed by β-galactosidase (see Miao below), but the reference does not explicitly state that C12FDG is used.

However, Miao et al teaches the following limitations that are deficient in Thompson et al:

For ***claims 11-12***, Miao et al (see entire document) explicitly teaches the use of "C12FDG" with a "lipophilic group" in assays using β-galactosidase like the one employed by Thompson et al (see Miao et al, abstract; see also page 708, column 2, paragraph 1).

It would have been obvious to one skilled in the art at the time the invention was to use the C12FDG as taught by Miao et al with the β-galactosidase enzyme reporter system as taught by Thompson et al because Miao et al explicitly states that the C12FDG substrate is specifically designed to be used in these types of assays with β-galactosidase. one would have been motivated to use the C12FDG because Miao et al explicitly states that the C12FDG contains a lipophilic group that allows the substrate to penetrate through the cell membrane, which would be advantageous because according to Miao et al, "This improvement provides a great increase in intracellular fluorescence intensity and a reduction in dye transfer among cells. By using this new substrate, it becomes possible to separately count β-galactosidase-positive (plasmid-bearing) and B-galactosidase-negative (plasmid-free) bacterial cells using flow cytometry" (see Miao et al, page 708, column 2, paragraph 1). One of skill in the art would have been reasonably assured of success because Miao et al shows a successful example using flow cytometry.

Double Patenting

20. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686

F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

21. Claim 1-20 and 22-26 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-23 of U.S. Patent No. 6,174,673 in view of Thompson et al.

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examiner application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1986).

Here, claims 1-23 of U.S. Patent No. 6,174,673 recites a method for screening a library of DNA clones derived from a mixed population of organisms using a fluorescent substrate. The '673 patent also recites encapsulation in a microdroplet, separation with a fluorescence analyzer, an expression library, extremophiles, bioactive substrates including C12FDG, normalization and enzymes including esterase as the polypeptide of interest. The method of claims 1-26 in the present application differ from claims 1-23 of '673 herein in that they fail to disclose the use of oligonucleotide probes. However, Thompson et al discloses the use of oligonucleotide probes

(see '673, column 37, line 33; see also Thompson et al section 5.2.3, especially column 37, lines 30-36, "The combinatorial gene expression libraries of the invention may be pre-screened or screened by a variety of methods, including but not limited to, visual inspection, automated image analysis, hybridization to molecular beacon DNA probes (Tyagi et al.1996, Nature Biotechnol,14:303-308) fluorescence activated cell sorting (FACS) and magnetic cell sorting (MACS)"). It would have been obvious to modify the method of claims 1-23 of U.S. Patent No. 6,174,673 to use oligonucleotide probes (e.g., molecular beacons) as taught by Thompson et al because the fluorescence signal generated by the molecular beacon DNA probes would help "identify a bioactivity or biomolecule" and thus fall within the scope of the preferred embodiment. One having ordinary skill in the art would have been motivated to make such a modification because the "molecular beacon DNA probes" taught by Thompson et al because Tyagi et al states that it is not necessary to remove the molecular beacons thus allowing them to be used in living cells, which would fall within the scope of Applicants' claimed microenvironment.

22. Claim 1-20 and 22-26 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-72 of U.S. Patent Application No. 2001/0041333 A1 (referred to as '333); Application No. 09/738,871.

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226

(Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1986).

Although the conflicting claims are not identical, they are not patentably distinct from each other (compare all claims of '333 to present application, especially those claims outlined below). For example, both inventions are directed to **[a]** a method for identifying a polynucleotide encoding a polypeptide of interest, **[b]** co-encapsulating in a microenvironment a plurality of library clones, **[c]** containing DNA obtained from a mixed population of organisms (compare claim 32 of '333 to claim 1 of the present application), **[d]** with a mixture of oligonucleotide probes comprising a fluorescence marker (compare claims 4 and 32 of '333 to claim 1 of the present application wherein '333 discloses a "fluorescent" marker), **[e]** and at least a portion of the polynucleotide sequence encoding a polypeptide of interest having a specified bioactivity under such conditions and for such time as to allow interaction of complementary sequences (compare claim 32 of '333 to claim 1 of the present application), **[f]** and identifying clones containing a complement to the oligonucleotide probe encoding the polypeptide of interest (compare claim 32 of '333 to claim 1 of the present application) and **[g]** by separating clones with a fluorescent analyzer that detects fluorescence (compare claims 32 and 63 of '333 to claims 1 and 5 of the present invention).

It would have been obvious to combine the claims of '333 to render obvious the claims of the present application because the claims of '333 teach a generic method (i.e., claims 1 and 32 are drawn to a method for identifying a polynucleotide and then further teaches more specific embodiments (i.e., the dependent claims teach more specific embodiments) that teach toward applicant's claimed invention.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Contact Information

23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (703) 308-2423. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-2439.

Jon D. Epperson, Ph.D.
August 7, 2003

BENNETT CELSA
PRIMARY EXAMINER